NARRATIVE: The focus of this proposal is to define the systemic and local immune responses to administration of adenovirus (Ad) gene transfer vectors to normal humans. It is the hypothesis of this proposal that intrabronchial administration of Ad vectors to normals will elicit local (lung epithelial) and systemic humoral and cellular immunity directed against the Ad vector, but that these anti-vector responses will be mild. To evaluate this hypothesis, a clinical study has been developed to define systemic and local immune responses to administration of an Ad vector to normal individuals. The vector to be used is Ad5CMV.Null2, and E1a$^-$, partial E1b$^-$, partial E3$^-$, Ad vector that is "null," i.e. it contains an expression cassette with a promotor, but no transgene (to eliminate the variable of the immune response against the transgene). The vector will be administered to the bronchial epithelium (one time, as well as repetitively, in ascending doses to different individuals), and the local (lung epithelial) and systemic humoral and cellular immune responses to the vector evaluated. The objectives of this study are (1) to define the local)lung epithelial) and systemic humoral and cellular immune responses to a single and repetitive intrabronchial administration of a replication-deficient Ad vector to normal individuals; (2) to examine the differences in the local and systemic humoral and cellular immune responses to an Ad vector elicited by intrabronchial compared to intradermal administration of the Ad vector to normal individuals (RCR 216-1198, "Immune Responses to Intradermal Administration of an Adenovirus Type 5 Gene Transfer Vector (Ad5CMV.Null2) in Normal Individuals").